Potassium Iodide for Cutaneous Inflammatory Disorders: A Monocentric, Retrospective Study

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Abstract: OBJECTIVES: Potassium iodide (KI) is a medication that has been used for decades in dermatology and it is mentioned as a treatment option in all major dermatology textbooks. Yet, there is little recent information on its efficacy. In our study, we wanted to retrospectively evaluate the therapy response to KI in our patients. METHODS: The hospital information system was searched for patients treated with KI at the Department of Dermatology (University Hospital Zurich) in the last 20 years (January 1, 1998 to December 31, 2017). A total of 52 patients were found and, subsequently, 35 patients were included in our study. RESULTS: KI was prescribed for the following skin conditions: erythema nodosum, disseminated granuloma anulare, necrobiosis lipoidica, nodular vasculitis, cutaneous sarcoidosis, and granulomatous perioral dermatitis/ rosacea. The median duration of KI intake was 5 ± 7.7 weeks (range 1-26). The global assessment of efficacy by the treating physician showed an improvement of disease in about a third of all patients. No response was seen in 14 patients and 9 even had a progression of disease. An adverse event was documented in 16 cases. CONCLUSIONS: Our findings show that an improvement was reached in only about a third of all cases. High response rates with only mild side effects (in 16 out of 35 patients) were observed.

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Potassium Iodide for Cutaneous Inflammatory Disorders: A Monocentric, Retrospective Study

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Keywords
Potassium iodide · Inflammatory dermatosis · Erythema nodosum · Necrobiosis lipoidica · Nodular vasculitis · Granuloma anulare

Abstract
Objectives: Potassium iodide (KI) is a medication that has been used for decades in dermatology and it is mentioned as a treatment option in all major dermatology textbooks. Yet, there is little recent information on its efficacy. In our study, we wanted to retrospectively evaluate the therapy response to KI in our patients. ***Methods:*** The hospital information system was searched for patients treated with KI at the Department of Dermatology (University Hospital Zurich) in the last 20 years (January 1, 1998 to December 31, 2017). A total of 52 patients were found and, subsequently, 35 patients were included in our study. ***Results:*** KI was prescribed for the following skin conditions: erythema nodosum, disseminated granuloma anulare, necrobiosis lipoidica, nodular vasculitis, cutaneous sarcoidosis, and granulomatous perioral dermatitis/ rosacea. The median duration of KI intake was 5 ± 7.7 weeks (range 1–26). The global assessment of efficacy by the treating physician showed an improvement of disease in about a third of all patients. No response was seen in 14 patients and 9 even had a progression of disease. An adverse event was documented in 16 cases. ***Conclusions:*** Our findings show that an improvement was reached in only about a third of all cases. High response rates with only mild side effects (in 16 out of 35 patients) were observed.

Introduction

Potassium iodide (KI) is a medication that has been used for decades in dermatology [1]. Kl is a photosensitive crystal composed of salt (76%) and potassium (23%) [2]. It was originally used to treat thyroid disorders and was then obtained from seaweed in ancient times. Its designated use encompassed diseases like psoriasis, eczema, tuberculosis, and syphilis [2, 3].

Nowadays, KI represents a treatment option in inflammatory, granulomatous, and infectious diseases, like erythema nodosum [4], nodular vasculitis [4], subacute migratory panniculitis [5], granuloma anulare [6, 7], pyoderma gangrenosum [8], granulomatosis with polyangiitis,

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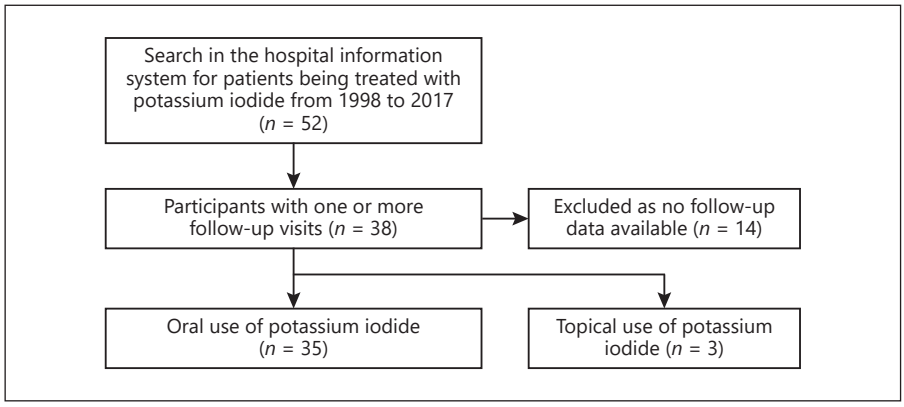

Fig. 1. Flowchart of Materials and Methods. Participant inclusion and exclusion.

Behçet's disease, Sweet's syndrome [1, 9], cryptococcosis [10], and zygomycosis [11]. Most studies have been performed on sporotrichosis [12–18]. KI has a fast effect on dermatosis. It is reported that remission occurs within days or weeks [19]. For inflammatory dermatosis, the recommended dosage is 300 mg three times daily [20].

Nondermatological indications include emphysema, cystic fibrosis, and cataract [2, 21–23]. It is controversial whether KI can be administered to patients with thyroid disease [1, 2, 19, 24, 25]. However, in case of a nuclear emergency, KI is used as a thyroid blocker [26]. Observed side effects include nausea, vomiting, and skin changes such as eczema and acneiform rashes [4]. An excess of iodine can cause thyrotoxicosis (Jod-Basedow effect) [20].

The absorption of iodine through the skin is poor, which makes it a commonly used topical disinfectant. When orally applied, KI is concentrated in the thyroid gland and excreted in urine, as well as feces. It has been proven to be teratogenic and should thus not be applied in pregnant women [2].

The precise mechanism of action has not been revealed [2]. However, it is assumed that its anti-inflammatory effects are partly exerted by the suppression of toxic oxygen, inhibition of chemotaxis, as well as by halogenation reactions from myeloperoxidases [27–29]. There is no direct antibacterial or antifungal activity [30].

Data on its efficacy are scarce, as only little interest exists from scientific centers and pharmaceutical companies. In fact, no randomized, placebo-controlled, or double-blind studies on its efficacy have been conducted [2]. Nonetheless, for more than a century clinical researchers have described its efficacy in multiple diseases. In our study, we wanted to retrospectively evaluate the efficacy of KI in our patients.

Table 1. Overview of patients' characteristics

Patients, *n*	35
Male	11
Female	24
Age, years	50±18 (18–79)

Data for age are presented as mean ± SD (range).

Materials and Methods

For further details, see the online supplementary material (see www.karger.com/doi/10.1159/000494614 for all online suppl. material) (Fig. 1).

Results

A total of 35 patients were included in our study (Table 1): 11 patients were diagnosed with disseminated granuloma anulare, 9 with erythema nodosum, 7 suffered from necrobiosis lipoidica, and 3 patients had a cutaneous manifestation of sarcoidosis. The remaining patients suffered from granulomatous perioral dermatitis or granulomatous rosacea (*n* = 3) and 2 were diagnosed with nodular vasculitis (Fig. 2; Table 2). In our cohort, there was no complete clearing: 12 out of 35 showed an improvement as judged by the physician, no response was seen in 14 patients, and 9 even had a progression of disease (Fig. 3a). From the 9 patients with erythema nodosum, 5 showed an improvement, and the remaining 4 did not benefit from this treatment (Fig. 3b; Table 2). On the contrary, all 3 patients with granulomatous perioral dermatitis or rosacea worsened during treatment. Similar re-

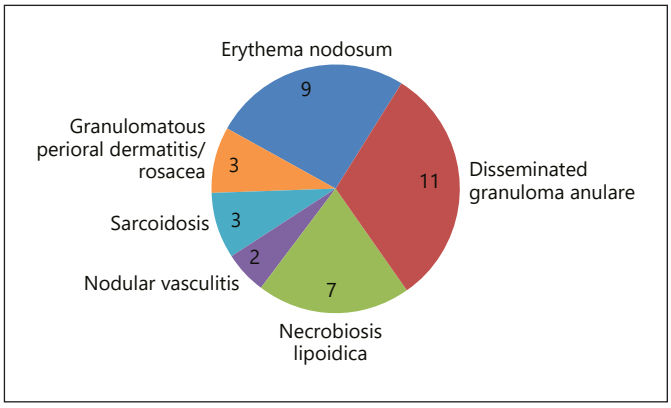

Fig. 2. Diseases treated with potassium iodide.

Table 2. Patients' response to treatment according to disease

	Total	Remission	Improvement	No response	Progression of disease
Erythema nodosum	9	0	5	3	1
Disseminated granuloma anulare	11	0	4	5	2
Necrobiosis lipoidica	7	0	2	5	0
Nodular vasculitis	2	0	1	0	1
Cutaneous sarcoidosis	3	0	0	1	2
Granulomatous perioral dermatitis/rosacea	3	0	0	0	3

Data are presented as number of patients.

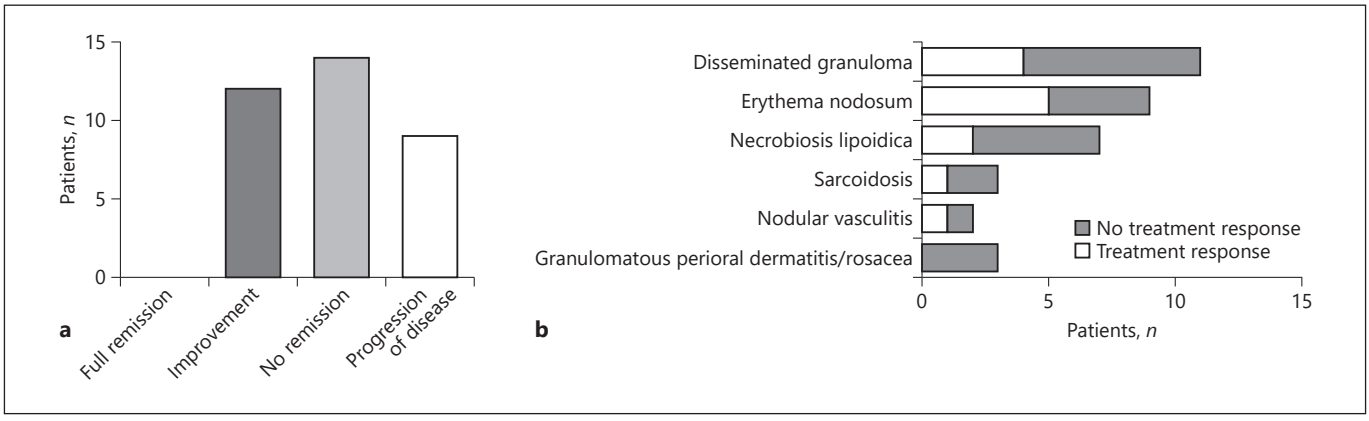

Fig. 3. a Treatment response to potassium iodide. **b** Treatment response stratified according to disease.

sults were seen in cutaneous sarcoidosis. Disseminated granuloma anulare showed an improvement in 4/11, necrobiosis lipoidica in 2/7, and nodular vasculitis in 1/2. An adverse event was documented in 16 cases, namely hypothyreosis, stomachache, palpitations, metallic sensation in the mouth, vertigo, obstipation, malaise, shivering, and hyperhidrosis. With the exception of hyperhidrosis and stomachache, which were Common Terminology Criteria (CTC) grade 2, all side effects were CTC grade 1. The median duration of KI intake was 5 ± 7.7 weeks, but ranged from 1 to 26 weeks. On average, 900 ± 389 mg (range 130–1,800) KI was administered daily; 3/35 patients suffered from diabetes mellitus. KI was never used as a first-line treatment. However, in 20/35 it was a second-line, in 7/35 a third-line, and in 4/35 a fourth-line treatment. It was never used as a fifth-line treatment and was used as a sixth-line treatment in 1 case. In almost all cases topical steroids were used as first-line treatments. Topical calcineurin inhibitors or systemic, immunomodulating antibiotics, such as dapsone or tetracyclines, were also used (Table 3).

Discussion/Conclusion

KI has been used in dermatology for a long time [1, 4]. The reports of Schulz and Whiting [31], where 24/28 patients suffering from erythema nodosum as well as 16/17 patients suffering from nodular vasculitis responded to therapy with KI, revived its use in modern clinics. The findings were confirmed by Horio et al. [4]. In fact, in some cases first signs of response were seen within 24 h,

Table 3. Patients' clinical characteristics

Age, years	Sex	Dosage (max)	Duration, weeks	Disease	Previous treatments	LOT	R	I	NR	POD	AE	CTC grade	TOT	DM
79	F	900 mg/d	4	disseminated granuloma anulare	TS, UVA1	3		x			hypothy-reosis		yes	no
48	F	900 mg/d	3	erythema nodosum	TS	2		x			no		yes	no
24	F	300 mg/d	9	necrobiosis lipoidica	TS	2		x			no		yes	no
69	F	900 mg/d	3	granulomatous perioral dermatitis/ rosacea	tacrolimus, SS, oral tetracyclines, topical macrolides	5				x	no		yes	no
72	F	900 mg/d	3	erythema nodosum	TS, SS				x		no		yes	yes
54	M	900 mg/d	1	granulomatous perioral dermatitis/ rosacea	topical pimecrolimus, oral tetracycline, oral nitroimidazole	4				x	stomachache	1	yes	no
68	M	1,500 mg/d	12	disseminated granuloma anulare	TS, UVA1, intra-lesional triamcinolon injections	4		x			no		no	no
50	M	900 mg/d	4	cutaneous sarcoidosis	TS (patient was under systemic tacrolimus, mycophenolat-mofetil)	2			x		no		no	no
45	F	900 mg/d	5	necrobiosis lipoidica	TS, topical pimecrolimus	3			x		palpation	1	no	no
55	F	900 mg/d	11	disseminated granuloma anulare	TS	2				x	metallic sensation in mouth	1	yes	no
63	F	600 mg/d	12	disseminated granuloma anulare	TS, UVA1	3			x		hypothy-reosis	1	yes	no
18	F	900 mg/d	36	disseminated granuloma anulare	TS	2			x		no		no	no
57	M	1,800 mg/d	9	disseminated granuloma anulare	TS, dapson	2				x	no		yes	no
72	F	900 mg/d	3	erythema nodosum	TS, SS	3				x	no		yes	no
29	F	900 mg/d	9	cutaneous sarcoidosis	TS	2				x	no		yes	no
45	F	1,800 mg/d	5	necrobiosis lipoidica	TS, topical pimecrolimus	2			x		palpation, hypothy-reosis	1	no	no
57	F	900 mg/d	8	erythema nodosum	TS, SS	3			x		no		yes	no
63	F	1,800 mg/d	6	disseminated granuloma anulare	TS	2			x		no		yes	no
54	F	900 mg/d	3	granulomatous perioral dermatitis/ rosacea	TS, topical tacrolimus, oral tetracyclines	4				x	stomachache	2	yes	no
38	M	600 mg/d	12	erythema nodosum	TS	2		x			no		no	no

Table 3 (continued)

Age, years	Sex	Dosage (max)	Duration, weeks	Disease	Previous treatments	LOT	R	I	NR	POD	AE	CTC grade	TOT	DM
19	F	900 mg/d	4	necrobiosis lipoidica	TS, topical pimecrolimus	3			x		no		yes	yes
50	M	900 mg/d	16	erythema nodosum	TS	2		x			no		no	no
73	F	300 mg/d	4	erythema nodosum	TS	2		x			vertigo	1	no	no
59	F	900 mg/d	4	disseminated granuloma anulare	TS	2		x			no		yes	no
35	M	900 mg/d	4	erythema nodosum	TS	2		x			no		no	no
72	F	900 mg/d	4	cutaneous sarcoidosis	TS	2				x	obstipation	1	yes	no
36	F	900 mg/d	4	erythema nodosum	TS	2			x		no		no	no
26	F	900 mg/d	4	nodular vasculitis	TS	2		x			hypothy-reosis		no	no
77	F	600 mg/d	24	disseminated granuloma anulare	TS	2		x			no	1	yes	no
36	F	900 mg/d	5	necrobiosis lipoidica	TS	2			x		no		yes	yes
55	M	900 mg/d	24	disseminated granuloma anulare	TS	2			x		malaise		yes	no
58	M	1,800 mg/d	6	disseminated granuloma anulare	TS, SS	3			x		no		yes	no
22	M	900 mg/d	1	necrobiosis lipoidica	TS, dapson, SS, MTX, UVA	6			x		no		yes	no
35	M	900 mg/d	20	necrobiosis lipoidica	TS, SS, pentoxifylline, topical pimecrolimus	4		x			hyperhi-drosis	2	no	no
51	F	130 mg/d	2	nodular vasculitis	TS, topical pimecrolimus	3				x	shivering	1	yes	no

LOT, line of treatment; R, remission; I, improvement; NR, no response; POD, progression of disease; AE, adverse events; TOT, termination of therapy at or before next consultation; DM, diabetes mellitus; d, day; TS, topical steroids; UVA, UV-A light therapy; SS, systemic steroids.

leading to high expectations of this treatment option [4, 20].

Unfortunately, our cohort yielded quite different results. Several factors could account for that. The study design of Schulz and Whiting [31] was prospective, while we performed a retrospective analysis. Also, the patient selection shows differences. Both studies included several patients with erythema nodosum, but our study also yields data on other diseases like necrobiosis lipoidica, granulomatous perioral dermatitis/rosacea, and cutaneous sarcoidosis. In the study of our colleagues, 17 patients were treated for nodular vasculitis, whereas our cohort only encompassed 2 such patients.

The probability of pharmacological differences seems to be rather low. As in the study of Schulz and Whiting, our patients received KI either in tablet form or as drops. The dose of KI in our patients was on average even higher than that in the cohort of Schulz and Whiting.

Our patients also received NSAIDs and topical steroids during the KI therapy in almost all cases, which would lead to the conclusion that our results would be superior to those previously published. In both studies (silent) malcompliance is a bias that cannot be ruled out, but we discovered only 5 cases of documented malcompliance in our cohort.

It has to be mentioned that for diagnoses like erythema nodosum and disseminated granuloma anulare (here KI showed the best treatment response in our study), we see a high rate of spontaneous remission in daily practice. Unfortunately, we cannot confirm our findings, as no data on the rates of spontaneous remission for those diseases exist.

As many scientists prefer to publish only positive data, publication bias may also be an explanation. Maybe other groups came to similar results as we did but abstained from publishing them. The small sample sizes in both studies may be a contributing bias.

Since there are no randomized, double-blind studies, and most of the existing studies have low numbers, it is difficult to make a final judgement with the evidence we have. Out of all dermatosis treated with KI, most of the existing data is on sporotrichosis [13–18], and the largest study included 645 patients [32]. Nonetheless, a Cochrane review found that even in this case, there is not enough (high-quality) evidence to come to a final conclusion regarding its efficacy [33].

In summary, in our opinion KI should not be first-line treatment. Depending on the disease, other therapeutic options should be sought first. Only in case of therapy refractory diseases and nonresponse to other first- and second-line therapeutics should KI be considered. Notably, in our cohort KI worked best in diseases with a high rate of spontaneous remissions, thus a double-blind study would be helpful to evaluate its efficacy.

It is surprising that our data differed from the previously published results. Nonetheless, we find it of high value to publish negative results to avoid a possible misconception by clinicians. In fact, we fear that due to publication bias many patients worldwide undergo treatment with KI, whose potential efficacy is, we believe, overestimated. In our view, this topic is of importance, as KI is mentioned as a treatment option in all well-known dermatology books, such as *Rook's Textbook of Dermatology*, *Fitzpatrick's Dermatology in General Medicine*, and *Dermatology* by Jean Bolognia.

We encourage other groups to analyze their treatment success with KI, but especially prospective, randomized, double-blind studies are needed to confirm the described effects of KI on dermatological diseases.

Key Message

Even though therapy with potassium iodide is mentioned in every major dermatology textbook, our cohort did not show high response rates such as those published previously.

Statement of Ethics

Subjects gave their written informed consent. The study protocol was approved by the research institute's committee on human research.

Disclosure Statement

The authors have no conflicts of interest to declare.

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